Complete Summary

GUIDELINE TITLE

NIH State-of-the-Science Conference Statement on management of menopause-related symptoms.

BIBLIOGRAPHIC SOURCE(S)

NIH State-of-the-Science Conference Statement on management of menopause-related symptoms. NIH Consens State Sci Statements 2005 Mar 21-23;22(1):1-38. PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Menopause

GUIDELINE CATEGORY

Evaluation
Management
Treatment

CLINICAL SPECIALTY

Family Practice
Geriatrics

Internal Medicine
Nursing
Obstetrics and Gynecology

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Health Care Providers
Nurses
Patients
Physician Assistants
Physicians

GUIDELINE OBJECTIVE(S)

To provide health care providers, patients, and the general public with a responsible assessment of currently available data on the management of menopause-related symptoms

TARGET POPULATION

Adult women in the United States undergoing the menopausal transition

INTERVENTIONS AND PRACTICES CONSIDERED

1. Symptoms in premenopausal, perimenopausal, and postmenopausal women
    - Vasomotor symptoms (hot flashes and night sweats)
    - Vaginal dryness and painful intercourse
    - Sleep disturbance
    - Mood symptoms
    - Cognitive disturbances
    - Somatic symptoms
    - Urinary incontinence
    - Uterine bleeding
    - Sexual dysfunction
    - Quality of life
2. Differentiation of symptoms of menopause from symptoms of aging
3. Estrogen therapy with or without progestin
    - Risks and benefits associated with estrogen therapy

Note: Interventions such as testosterone, dehydroepiandrosterone, bioidentical hormones, tibolone, antidepressants, clonidine, gabapentin, methyldopa, bellergal, isoflavones and other phytoestrogens, complementary and alternative approaches, and behavioral interventions were considered but not recommended.

MAJOR OUTCOMES CONSIDERED

- Sexual dysfunction
- Relief of symptoms
- Quality of life
- Side effects of therapy

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases
Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): A systematic review of the literature was prepared by the Oregon Evidence-based Practice Center for the Agency for Healthcare Research and Quality's Evidence-based Practice Centers Program for use by the National Institutes of Health (see the "Availability of Companion Documents" field).

The systematic review of the literature focused on five Key Questions relating to symptoms of menopause and their management, as specified by the Planning Committee for the National Institutes of Health State-of-the-Science Conference on Management of Menopause-Related Symptoms.

Relevant studies were identified from multiple searches of MEDLINE®, PsycINFO, DARE, the Cochrane database of systematic reviews and controlled trials, MANTIS, and AMED (1953 to November 2004); and from recent systematic reviews, reference lists, reviews, editorials, websites, and experts. Retrieved abstracts were entered into an electronic database (EndNote®).

Specific inclusion and exclusion criteria were developed to determine study eligibility for Key Questions 1-4:

1. What is the evidence that the symptoms more frequently reported by middle-aged women are attributable to ovarian aging and senescence?
2. When do the menopausal symptoms appear, how long do they persist and with what frequency and severity, and what is known about the factors that influence them?
3. What is the evidence for the benefits and harms of commonly used interventions for relief of menopause-related symptoms?
4. What are the important considerations in managing menopause-related symptoms in women with clinical characteristics or circumstances that may complicate decision-making?

Full text cohort studies with data on women experiencing menopause and at least one of the symptoms listed in Key Question 1 were initially reviewed and subsequently included if the study enrolled 100 or more subjects, subjects represented the target population, and data on symptoms associated with menopause were provided. Exclusions included studies of women not undergoing the menopausal transition and experiencing menopause related symptoms, studies of aging and its effects, and biologically based studies that did not report epidemiological data relating to symptoms (e.g., studies of hormone levels). Non-English language papers and studies of animals or cadavers were also excluded.

Cross-sectional studies meeting similar inclusion/exclusion criteria were examined for contributory data and included if they reported relevant data about symptoms by menopausal stage, such as prevalence rates.

Full text randomized controlled trials and meta-analyses of randomized controlled trials providing data on treatment of menopausal symptoms, using one or more of the interventions listed in Key Question 3, were included. Trials enrolling women with breast cancer were considered separately from those enrolling women without breast cancer. Exclusions included studies of women not undergoing menopause and experiencing menopause related symptoms during the course of the study, studies of animals, and non-English language papers. For this report, abstracts of unpublished trials are included in evidence tables, but not in summary tables and text.

Refer to Chapter 2 in the Evidence Report (see the "Availability of Companion Documents" field) for further information.

NUMBER OF SOURCE DOCUMENTS

- Key Questions 1 and 2 (symptoms and factors): 71 articles
- Key Question 3 (interventions): 134 articles
- Key Question 4 (characteristics): 15 articles

Refer to Appendix E "Literature Search Tree' in the Evidence Report (see the "Availability of Companion Documents" field) for additional information on source documents.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Not Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Note from the National Guideline Clearinghouse (NGC): A systematic review of the literature was prepared by the Oregon Evidence-based Practice Center for the Agency for Healthcare Research and Quality's Evidence-based Practice Centers Program for use by the National Institutes of Health (see the "Availability of Companion Documents" field).

All eligible studies were reviewed and a "best evidence" approach was applied, in which studies with the highest quality and most rigorous design are emphasized.

Data were extracted from each study, entered directly into evidence tables, and summarized descriptively. Benefits and adverse effects of therapies were considered equally important and both types of outcomes were abstracted. Trials of alternative and complementary therapies were grouped according to the National Center for Complementary and Alternative Medicine categories most closely related to included topics. Results of recently published meta-analyses on estrogens and isoflavones are included in this report. No new meta-analyses were conducted because of heterogeneity of trials of other therapies.

Two reviewers independently rated the quality of randomized controlled trials and cohort studies using criteria specific to different study designs developed by the United States Preventive Services Task Force (refer to Fig. 3. in the Evidence Report [see the "Availability of Companion Documents" field]). Similar criteria for cross-sectional studies are not available. The overall rating is a combination of internal and external validity scores. When reviewers disagreed, a final rating was reached through consensus. Studies reporting several different outcomes may have different quality ratings for each outcome depending on how well it measured the symptom and how completely it controlled for key confounders in multivariable models.

Refer to Chapter 2 in the Evidence Report (see the "Availability of Companion Documents" field) for further information.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Consensus Development Conference)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

This systematic evidence review focuses on five Key Questions relating to symptoms of menopause and their management, as specified by the Planning Committee for the National Institutes of Health State-of-the-Science Conference on Management of Menopause-Related Symptoms held on 21–23 March 2005, in Bethesda, Maryland.

A Technical Expert Panel was assembled to provide input from experts and clinicians in the field to ensure that the scope of the project addressed important clinical questions and issues. The panel included obstetrician/gynecologists, internists, naturopathic physicians, behavioral experts, and researchers. The panel was convened for periodic conference calls during the course of the project. Expert reviewers, including several panel members, provided comments on the draft evidence report.

An impartial, independent panel was charged with reviewing the available published literature in advance of the conference, including a systematic literature review commissioned through the Agency for Healthcare Research and Quality.

Answering the Key Questions below, the non-Department of Health and Human Services, nonadvocate 12-member panel representing the fields of obstetrics and gynecology, general internal medicine, endocrinology, rheumatology, family and

health psychology, geriatric medicine, health services research, demography, biochemistry, epidemiology, clinical research, and biostatistics drafted a statement based on scientific evidence presented in open forum and on the published scientific literature:

- What is the evidence that the symptoms more frequently reported by middle-aged women are attributable to ovarian aging and senescence?
- When do the menopausal symptoms occur, how long do they persist and with what frequency and severity, and what is known about the factors that influence them?
- What is the evidence for the benefits and harms of commonly used interventions for relief of menopause-related symptoms?
- What are the important considerations in managing menopause-related symptoms in women with clinical characteristics or circumstances that may complicate decision-making?
- What are the future research directions for treatment of menopause-related symptoms and conditions?

The draft statement was read in its entirety on the final day of the conference and circulated to the audience for comment. The panel then met in executive session to consider the comments received, and released a revised statement later that day at http://consensus.nih.gov.

Refer to the original guideline document and Chapter 2 in the Evidence Report (see the "Availability of Companion Documents" field) for further information.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Menopause is the permanent cessation of menstrual periods that occurs naturally in women, usually in their early 50s. Many women have few or no symptoms; these women are not in need of medical treatment.

Premenopausal or perimenopausal women who have menopause induced by surgery, chemotherapy, or radiation are more likely to experience bothersome and even disabling symptoms. These women need safe and effective treatment.

It is difficult to differentiate those symptoms that are truly associated with menopause from those due to aging. Hot flashes, night sweats, and vaginal dryness are clearly tied to the menopausal transition, and there is some positive evidence of a menopausal link for sleep disturbance.

Vasomotor symptoms are reported with high frequency during the menopausal transition.

Estrogen, either by itself or with progestins, is the most consistently effective therapy for these symptoms. However, the Women's Health Initiative (WHI) has identified important risks associated with use of these therapies. Decision making for women regarding treatment for menopausal symptoms requires personal knowledge and balancing of these risks.

There are many potential alternatives to estrogen. However, their effectiveness and long-term safety need to be studied in rigorous clinical trials in diverse populations of women.

To address the charge to this panel, much more research is needed to clearly define the natural history of menopause, associated symptoms, and effectiveness and safety of treatments for bothersome symptoms. Natural histories are important for both science and policy. Knowing how many women transit menopause with few or no symptoms, and how many manage menopause largely on their own, can lead to public health information that empowers women and increases their self-reliance. Medical care and future clinical trials are best focused on women with the most severe and prolonged symptoms.

The state of the science in management of menopausal symptoms should be reassessed periodically.

Menopause is "medicalized" in contemporary U.S. society. There is great need to develop and disseminate information that emphasizes menopause as a normal, healthy phase of women's lives and promotes its demedicalization. Medical care and future clinical trials are best focused on women with the most severe and prolonged symptoms. Barriers to professional care for these women should be removed.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is not specifically stated for each recommendation.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate management and treatment of menopause-related symptoms

POTENTIAL HARMS

Estrogen (Hormone Therapy)

- Breast tenderness and uterine bleeding are the most commonly reported adverse outcomes in estrogen trials; others include nausea and vomiting, headache, weight change, dizziness, venous thromboembolic events, cardiovascular events, rash and pruritus, cholecystitis, and liver effects.
- Estrogen therapy at doses equivalent to 0.625 mg of conjugated equine estrogen increases the risk for serious disease events, specifically stroke; deep venous thrombosis, pulmonary embolism, or both; and, when combined with progestin medroxyprogesterone acetate, coronary events and breast cancer. In studies in which women were treated for 5 to 7 years, increased risks for coronary and thromboembolic events started to emerge in the first year of use. Risks for stroke started to increase after 2 years of use. Risks for breast cancer started to increase after 3 to 4 years of use.
- Results from two large studies of oral estrogen, either alone or with progestins, showed increased risk for the development of urinary incontinence and for its worsening in women who were already experiencing it.

Antidepressants

Known adverse effects for antidepressants include diminished libido, insomnia, headache, and nausea. Long-term effects are unknown.

Other Medications

- Gabapentin was associated with greater somnolence, dizziness, rash, and peripheral edema.
- Clonidine was associated with greater difficulty sleeping compared with placebo.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- The statement reflects the panel's assessment of medical knowledge available at the time the statement was written. Thus, it provides a "snapshot in time" of the state of knowledge on the conference topic. When reading the statement, keep in mind that new knowledge is inevitably accumulating through medical research.
- This statement is an independent report of the panel and is not a policy statement of the National Institutes of Health (NIH) or the Federal Government. A final copy of this statement is available, along with other recent conference statements, at the same web address of http://consensus.nih.gov.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

NIH State-of-the-Science Conference Statement on management of menopause-related symptoms. NIH Consens State Sci Statements 2005 Mar 21-23;22(1):1-38. PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2005 Mar

GUIDELINE DEVELOPER(S)

National Institutes of Health (NIH) State-of-the-Science Panel - Independent Expert Panel

SOURCE(S) OF FUNDING

United States Government

GUIDELINE COMMITTEE

National Institutes of Health State-of-the-Science Panel

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Panel Members: Carol M. Mangione, M.D., M.S.P.H., (*Conference and Panel Chairperson*), Director, Resource Center for Minority Aging Research, Professor of Medicine, David Geffen School of Medicine at University of California, Los Angeles, Los Angeles, California; Deborah Briceland-Betts, J.D., Senior Vice President, Sutton Group—Solutions for Social Change, Washington, DC; Susan S. Ellenberg, Ph.D., Professor of Biostatistics, Center for Clinical Epidemiology and Biostatistics, Associate Dean for Clinical Research University of Pennsylvania, School of Medicine, Philadelphia, Pennsylvania; Scott S. Emerson, M.D., Ph.D., Professor and Graduate Program Coordinator, Department of Biostatistics, University of Washington, Seattle, Washington; David V. Espino, M.D., Vice Chair for Community Geriatrics, Department of Family and Community Medicine, University of Texas Health Science Center at San Antonio, San Antonio, Texas; Rose S. Fife, M.D., Associate Dean for Research, Professor of Medicine and Professor of Biochemistry and Molecular Biology; Barbara F. Kampen Professor of Women's Health, Indiana University School of Medicine, Indianapolis, Indiana; Susan Folkman, Ph.D., Professor of Medicine, Osher Foundation Distinguished Professor in Integrative Medicine, Director, Osher Center for Integrative Medicine, University of California, San Francisco, San Francisco, California; Cassandra E. Henderson, M.D., Associate Professor of Obstetrics and Gynecology, New York Medical College, Medical and Laboratory, Director at MIC–Women's Health Services, Chief of Maternal Fetal Medicine, Our Lady of Mercy Medical Center, Bronx, New York; Susan H. McDaniel, Ph.D., Professor of Psychiatry and Family Medicine; Director, Wynne Center for Family Research, Associate Chair Department of Family Medicine, University of Rochester School of Medicine and Dentistry, Rochester, New York; Lois M. Verbrugge, Ph.D., M.P.H., Visiting Professor, Asia Research Institute, National University of Singapore, Singapore Research Professor and Senior Distinguished Research Scientist, Institute of Gerontology, University of Michigan, Ann Arbor, Michigan; Donna L. Washington, M.D., M.P.H., Associate Professor of Medicine, VA Greater Los Angeles Healthcare System and University of California, Los Angeles, Los Angeles, California; Paul D. Woolf, M.D., M.B.A., F.A.C.P., Chairman, Department of Medicine, Crozer Chester Medical Center, Upland, Pennsylvania

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

All of the panelists who participated in this conference and contributed to the writing of this statement were identified as having no financial or scientific conflict of interest, and all signed forms attesting to this fact. Unlike the expert speakers who present scientific data at the conference, the individuals invited to participate

on NIH Consensus and State-of-the-Science panels are reviewed prior to selection to assure that they are not proponents of an advocacy position with regard to the topic and are not identified with research that could be used to answer the conference questions.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the National Institutes of Health (NIH) Consensus Development Conference Program Web site.

Print copies: Available from the NIH Consensus Development Program Information Center, PO Box 2577, Kensington, MD 20891; Toll free phone (in U.S.), 1-888-NIH-CONSENSUS (1-888-644-2667); autofax (in U.S.), 1-888-NIH-CONSENSUS (1-888-644-2667); e-mail: consensus_statements@mail.nih.gov.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- NIH State-of-the-Science Conference on Management of Menopause-Related Symptoms. 2005 Mar. 157 p. Available in Portable Document Format (PDF) from the National Institutes of Health (NIH) Consensus Development Conference Program Web site.
- Management of menopause-related symptoms. 2005 Mar. Available from the AHRQ Web site.

PATIENT RESOURCES

None available

NGC STATUS

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